Remarks

Claims 35-37, 39 and 57-94 are pending in the subject application. By this Amendment, Applicants have amended claims 35, 59, 64-66, 69, 72, 77-79, 82, 85 and 90-92. Support for the amendments can be found throughout the subject specification and in the claims as originally filed (see, for example, the original and previously presented claims, page 4 of the specification, the Examples and the Sequence Listing). Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 35-37, 39 and 57-94 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

As an initial matter, Applicants gratefully acknowledge the Examiner's withdrawal of the rejections under 35 U.S.C. § 102(b).

Claims 35-37, 39 and 57-94 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Office Action indicates that the remarks previously presented were not found persuasive and states that adequate written description is conferred by correlation between structure and function. The Office Action further argues that the claims are drawn to a genus of polypeptides that are defined by their functionality and that fusion proteins, active mutants and peptides of between 5 and 10 amino acids that bind OX40R do not have adequate written description. Applicants traverse.

At the outset, Applicants note that each of the polypeptides that are alleged to lack adequate written description are defined by both structure and function. For example, claim 35 recites:

An isolated polypeptide consisting of:

a) amino acids 94-124 of human OX40 ligand (OX40L);

b) amino acids 94-124 of human OX40L, wherein one or more amino acids have been deleted, said polypeptide contains amino acids 107-111 of human OX40L and said polypeptide binds to the OX40 receptor (OX40R);

c) between 5 and 10 contiguous amino acids of OX40L, wherein said polypeptide contains amino acids 107-111 of OX40L and binds to OX40R;

d) amino acids 107-116 or 107-111 of human OX40L;

e) an active mutant of a), b), c) or d), wherein one or more of the amino acids has been conservatively substituted and said active mutant binds to OX40R;

f) a fusion polypeptide or peptide comprising a protein sequence other than human OX40L fused to:

i) a peptide consisting of amino acids 94-124 of human OX40L;

ii) a peptide consisting of amino acids 94-124 of OX40L, wherein one or more amino acids have been deleted, said peptide contains amino acids 107-111 and said fusion polypeptide binds OX40R;

iii) an amino acid sequence of between 5 and 10 contiguous amino acids of OX40L that includes amino acids 107-111 of OX40L and said fusion polypeptide binds to OX40R;

iv) a peptide consisting of amino acids 107-116 or 107-111of human OX40L; or

g) a derivative of a), b), c), d), e) or f).

As will be noted from the claims, each of the claim subparts recite peptides that have structural limitations or both structural and functional limitations. For example, subpart c) recites a peptide consisting of between 5 and 10 contiguous amino acids of OX40L, wherein said polypeptide contains amino acids 107-111 of OX40L and binds to OX40R. Thus, this polypeptide corresponds to 5-10 amino acids of OX40L that include amino acids 107-111 of the polypeptide (identified as SEQ ID NO: 1). Thus, it is respectfully submitted that adequate written description of this peptide exists in the as-filed specification. Likewise, fusion proteins containing such a peptide have adequate written description.

With respect to derivatives of the claimed polypeptides, it is respectfully submitted that these peptides are adequately described. For example, derivatives are defined at page 14 and refer "to derivatives which can be prepared from the functional groups present on the lateral chains of the amino acid moieties or on the N-/ or C-terminal groups according to known methods. Such derivatives include for example esters or aliphatic amides of the carboxyl-groups and N-acyl derivatives of free amino groups or O-acyl derivatives of free hydroxyl-groups and are formed with

acyl-groups as for example alcanoyl- or aroyl-groups". Thus, it is respectfully submitted that the as-filed specification and claims conform to the written description requirement of section 112.

Finally, the Office Action argues that active mutants of the claimed polypeptides are not supported by the as-filed specification. In this regard, Applicants again respectfully traverse. The as-filed specification indicates that the OX40R binding portion of the disclosed peptides is associated with amino acids 107-111 of SEQ ID NO: 13 (see Example 2, page 36, lines 11-15 and Figure 6). Further, the as-filed specification discloses a number of peptides having the recited characteristics (see Example 2). Additionally, the as-filed specification (at pages 9-10) provides teaching as to substitutions that can be made within the claimed peptides and methods of screening the peptides for activity (OX40R binding) are also disclosed in the application. Applicants also note that the term "active" is defined in the as-filed specification as a compound demonstrating the OX40R binding properties of the peptides disclosed within the as-filed application (see page 9, lines 9-10). Applicants also note that the claims indicate that the active mutants of the claimed polypeptides must also bind to OX40R and, thus, contain amino acids 107-111. Thus, it is respectfully submitted that the claimed polypeptides are defined both structurally and functionally and that adequate written description of the claimed polypeptides was provided in the as-filed specification. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Claims 35-37, 39 and 57-94 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite. The Office Action argues that it is unclear as to whether the phrase "one or more" may include a situation in which all the amino acids may be substituted. Applicants respectfully submit that the claims are definite and that one skilled in the art, in view of the teachings of the as-filed specification, would be able to ascertain the metes and bounds of the claimed invention. For example, the claims in question indicate that the claimed polypeptides contain amino acids 107-111 of the OX40L and the peptide binds to OX40R; thus, it is clear that not all amino acids are substituted. With respect to the alleged clarity issues noted as to whether the peptides are derived from human OX40L, Applicants note that the sequence listing indicates that the various peptides are derived from human OX40L (see SEQ ID NOs: 1-13) and the as-filed specification at page 4, lines 10-20 clearly indicate that the claimed peptides are derived from human OX40L. However, in the

interest of advancing prosecution in this matter, the claims have been amended to resolve these issues and reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested.

Claims 35-37, 39 and 57-94 are rejected under 35 U.S.C. § 103(a) as obvious over Godfrey *et al.* (U.S. Patent No. 6,242,566) in view of Chien *et al.* (1991). The Office Action asserts that Godfrey *et al.* teach purified ACT-4-L ligand polypeptides; an exemplified ACT-4-L ligand designated ACT-4-l-h-1. In addition, it is stated that Godfrey *et al.* teach purified extracellular domains of ACT-4-L ligands. The Office Action cites Chien *et al.* as teaching a method by which a protein-protein interaction is indentified in vivo through reconstitution of the activity of a transcriptional activator. Applicants note that the Office Action also asserts that the claimed invention is obvious and that one skilled in the art would have arrived at the domains essential to the binding of ACT 4L to its receptor because the domain to be searched was disclosed by Godfrey *et al.*, the search would have entailed a finite number of fragments already envisioned (in length). Applicants respectfully traverse the rejection and submit that a *prima facie* case of obviousness has not been established by the Patent Office.

At the outset, Applicants note that the obviousness rejection of record appears to rely on the rationale articulated in *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007) in establishing the rejection of record. Applicants also note that the Patent Office's guidelines promulgated in light of the KSR decision also provide a similar rationale for establishing an obviousness rejection (see 72 Fed. Reg. 57526, 57532). Applicants further note that the full quote of that portion of the KSR decision which appears to serve as the basis of the instant rejection states that "[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." Further, the Patent Office guidelines state (at page 57532):

> E. "Obvious To Try"—Choosing From a Finite Number of Identified, Predictable Solutions, With a Reasonable Expectation of Success

> To reject a claim based on this rationale, Office personnel must resolve the *Graham* factual inquiries. Office personnel must then articulate the following:
>
> (1) a finding that at the time of the invention, there had been a recognized problem or need in the art, which may include a design need or market pressure to solve a problem;
> (2) a finding that there had been a finite number of identified, predictable potential solutions to the recognized need or problem;
> (3) a finding that one of ordinary skill in the art could have pursued the known potential solutions with a reasonable expectation of success; and
> (4) whatever additional findings based on the *Graham* factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness.

In this case, Applicants respectfully submit that the Patent Office has failed to establish the *prima facie* obviousness of the claimed invention as the rejection of record fails to meet the requirements of either the KSR decision or the guidelines promulgated by the Patent Office. Namely, the Patent Office has failed to establish that there was a recognized problem or need in the art to solve a problem that would have motivated one to even try to identify peptides corresponding to those claimed in this matter. Further, the Patent Office has failed to establish that there was a finite number of identified, predictable solutions for solving the recognized need or problem. It is noted that the Office Action argues that there are a finite number of peptide fragments that can be generated in light of the teachings of Godfrey *et al.*; however, it is clear that thousands or tens of thousands of possible fragments could be generated and no finding as to which of those fragments would have predictably solved the problem (which is, as of yet, unidentified by the Patent Office). Accordingly reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a) is respectfully requested as a *prima facie* case of obviousness has not been established in this matter.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including

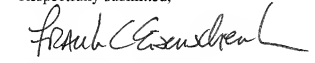
any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



Frank C. Eisenschenk, Ph.D.
Patent Attorney
Registration No. 45,332
Phone No.: 352-375-8100
Fax No.: 352-372-5800
Address: P.O. Box 142950
Gainesville, FL 32614-2950

FCE/sl